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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/398,897	09/20/99	YANG R	0109015/016

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EXAMINER	
HAYES,R	
ART UNIT	**PAPER NUMBER**
1647	5

DATE MAILED: 07/16/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/398,897	Yang et al
Examiner	**Art Unit**
Robert C. Hayes	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Apr 30, 2001 .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above, claim(s) 6-11 and 17-22 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-5 and 12-16 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims 1-22 are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I in Paper No. 4 is acknowledged. The traversal is on the ground(s) that the products must be rejoined with the method of Group I if they cannot be made by an alternative process. This is not found persuasive because the multipotent neural stem cells of Group II, or glial-restricted precursor cells of Group III or the neuronal-restricted cells of Group IV can all be produced by different methods that also involve transfection with the c-myc gene. For example, different methods do not require serum-free medium, nor two separate treatments with either FGF, EGF or TGFα. Moreover, because each of these distinct populations of cells possess their own unique characteristics and/or differentiation potential, in which transfection with a c-myc construct merely allows one to more easily propagate stable cell line, each of these different populations of cells are also distinct from each other, and vice versa. It is further noted that the method of Group I does not distinguish how to produce the glial-restricted precursor cell of Group III or the neuronal-restricted cells of Group IV, versus the multipotent neural stem cells of Group II, and vice versa. Therefore, these groups are distinct for the reasons made of record. The requirement is still deemed proper and is therefore made FINAL.

Claims 6-11 & 17-22 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected inventions, the requirement having been traversed in Paper No. 4.

This application contains claims 6-11 & 17-22 are drawn to an invention nonelected with traverse in Paper No. 4. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Specification

2. The spacing of the lines of the specification is such as to make reading and entry of amendments difficult. New application papers with lines double spaced on good quality paper are required.

Information Disclosure Statement

3. The information disclosure statement filed 1/30/00 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 & 12-16 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The c-myc construct, c-myc *gene*, or "other DNA elements", required for carrying out step (c) critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

The specification discloses a cartoon of a construct containing the c-myc proto-oncogene as Figure 1. No sequence information nor proper citation of references on what exactly constitutes this construct, or any "c-myc *gene*", which is required to practice the instant method of producing stable neural precursor cells, is described. Therefore, without an adequate written description on what structurally constitutes the necessary c-myc constructs, the c-myc *gene*, along with the "other DNA elements" recited in claims 2 & 13, the skilled artisan would not know how to make and use Applicants' invention without requiring undue experimentation to determine such.

Applicant is also directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999.

5. Claims 1-5 & 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is ambiguous what metes and bounds constitutes "an *agent*

capable of being taken up by the cells and capable of expressing a c-myc *gene*", when no c-myc "gene" is described in the specification and the only possible "agent" appears to be a c-myc cDNA construct, which itself is not described within the specification. Moreover, if a c-myc construct is not "taken up by the cells", it could not "express" anything (i.e., as it relates to the recitation, "capable of").

6. Claims 1-5 & 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: whether an additional reporter construct is necessary that contains the "ligand binding domains", such that a c-myc construct can be activated. In other words, what context can "ligand binding domains" fused to a c-myc cDNA molecule accomplish anything that works in the proposed method? What construct contains the steroid hormone receptor "DNA binding domains", in order to have a method that works?

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-5, 12 & 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. (U.S. Patent 5,580,777), in view of Weiss et al. (U.S. Patent 5,851,832).

Bernard et al. teach a method for producing stable cell lines of mammalian neural precursor/neuroepithelial/neural crest/pluripotent embryonic stem cells *in vitro* comprising transfection with a retroviral construct comprising the c-myc proto-oncogene and the selectable marker Neo^R gene for G418 (cols. 4-5; as it relates to claims 1a, 1c, 12a & 12c)). Transfected cells were further cultured with aFGF or bFGF to induce differentiation (col. 12, line 42-64; as it relates to the second mitogen of claims 1d & 12d). Co-cultures of these cells using an irradiated feeder layer of 3T3 fibroblasts is also taught by Bernard (col.5, lines 15-17; col. 11, lines 7-30; as it relates to claim 12e), which can also aid in the differentiation of these cells to neurons and glia. However, Bernard et al. do not teach initial culturing of these neural precursor cells in medium that is serum-free.

Weiss et al. teach that "a preferred embodiment for proliferation of neural stem cells is to use a defined serum-free culture medium, as serum tends to induce differentiation and contains unknown components" (col. 16, lines 23-26; as it relates to claims 1a & 12a). "The culture

medium is supplemented with at least one proliferation-inducing growth factor" (col. 16, lines 41-42), in which "[p]referred proliferation-inducing growth factors include EGF and TGFα" (col. 16, lines 56-57; as it relates to claims 1b & 12b). Weiss also teach use of human pluripotent embryonic stem cells (cols. 13 & 15-16; as it relates to claims 4-5 & 15-16). However, Weiss et al. do not disclose transfection of neural precursor/stem cells with c-myc constructs to form stable cell lines.

It would have been obvious to one of ordinary skill in the art at the time of filing Applicants' invention to modify Bernard's method of producing neural precursor/stem cells by using serum-free medium, and culturing Bernard's neural precursor cells in the presence of the first mitogen, EGF or TGFα, as taught by Weiss, in order to prevent premature differentiation of these neural precursor cells (which include Weiss' human pluripotent embryonic stem cells; as it relates to claims 4-5 & 15-16) prior to being transfected with Bernard's c-myc construct that immortalizes these cells. Bernard's step (d) can subsequently be carried out using the second mitogens, aFGF or bFGF, to more accurately determine the effects of these defined components on the differentiation potential to neuronal-restricted cells, or alteratively to glial-restricted cells, etc., or to determine any of the other potential uses suggested by Bernard in column 13.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
March 15, 2001

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